

**REMARKS**

Claims 37, 39, 41-46 and 55 were previously pending in this application. By this amendment, claim 37 has been amended. As a result claims 37, 39, 41-46 and 55 are pending for examination with claim 37 being an independent claim. Support for the amendments to the specification and claims are supported by the specification as filed, particularly in the first paragraph of the specification, the last full paragraph on page 6, the 4<sup>th</sup>-6<sup>th</sup> full paragraphs on page 7, the 3<sup>rd</sup> and 4<sup>th</sup> full paragraphs on page 8, the paragraph bridging pages 9 and 10, and the first full paragraph on page 10. No new matter has been added.

The first paragraph of the specification indicates that the invention pertains to adjuvant compositions and methods for stimulating or enhancing immunogenic effects of antigens co-administered with the adjuvant compositions; this passage clearly contemplates administering antigens that are not pertussis toxin, which is used as the adjuvant, because if the pertussis toxin adjuvant were also the antigen, there would be no need to co-administer an antigen. The last full paragraph on page 6 supports this conclusion, particularly when viewed in combination with the preceding paragraph, which concerns the use of the non-toxic double mutant form of pertussis toxin and an antigen to induce an immune response against B. pertussis infection, as compared to stimulating or enhancing a protective immune response of the co-administered antigen.

Note also the features of adjuvant compositions and methods include both an antigen (sometimes referred to as a first antigen) and the pertussis toxin double mutant (in its role as the adjuvant). For example, the first full paragraph on page 10 indicates that the pertussis toxin double mutant can be administered with a C fragment of tetanus toxin in order to enhance the immunogenicity of the C fragment.

**Claim Rejections Under 35 U.S.C. § 103**

The Examiner maintained the rejection of claims 37, 39, 41-46 and 55 under 35 U.S.C. § 103(a) as unpatentable over Nencioni et al. and Podda et al. in view of Capiau et al., Tamura et

al. and Honda et al. Reconsideration of the rejection of claims 37, 39, 41-46 and 55 under 35 U.S.C. § 103(a) is requested in view of the amendment of claim 37.

Assuming for the present that the combination of references is appropriate (which is not conceded by any means), the invention as now claimed would not have been obvious from the combined teachings of the references. The combination of references does not teach or suggest that the double mutant toxin recited in the claims would act as an adjuvant to stimulate or enhance a protective immune response to an antigen when administered by a mucosal route. As noted in the previously filed response to the Final Office Action, the adjuvant activity of pertussis toxin was perceived to those of skill in the art as likely to be inseparable from its enzymatic activity (see Roberts et al. (1995) *Infection and Immunity* 63, 2100-2108, of record).

Concerning the Honda reference, as noted in the previously filed response to the Final Office Action, it was subsequently shown in the literature that allegedly pure preparations of the B subunit such as that described in Honda et al. were in fact contaminated by very small amounts of active pertussis toxin containing the S1/A subunit and that it was these very small amounts of active pertussis toxin that were responsible for the adjuvant activity.

Applicant also notes the unexpected effectiveness (explained in greater detail in previous responses) of the double mutant pertussis toxin recited in the claims as an adjuvant when administered by a mucosal route. This unexpected effectiveness further favors a finding of non-obviousness.

Based on the cited prior art, one of ordinary skill in the art would not have been motivated to use a double mutant pertussis toxin as is presently claimed.

In conclusion, the combination of the prior art cited by the Examiner does not provide the elements of Applicant's claimed invention. In particular, Nencioni et al. and Podda et al.

teach antigen activity of the mutant pertussis toxin but not any adjuvant activity, and the results of Honda et al. have been discredited with respect to their teachings of adjuvant activity attributable to pertussis toxin B subunit. The teachings of the other cited references do not, in combination, provide the elements missing from Nencioni et al., Podda et al. and Honda et al.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. 103(a).

**CONCLUSION**

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,  
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Docket No. M0975.70006US00  
Date: January 8, 2004  
X01/08/04